PROTRACTED LOW DOSE PHOTON AND SIMULATED SOLAR FLARE PROTON EFFECTS ON CYTOKINE/CHEMOKINE EXPRESSION AFTER WHOLE-BODY IRRADIATION

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Astronauts are exposed to low dose/low dose rate radiation (LDR) and may also be acutely irradiated during a solar particle event (SPE). The biological effects of LDR alone and when combined with a solar particle event, are not yet clearly understood. Previous studies have shown that irradiation can have adverse effects on T cells. The reactive oxygen species (ROS) that are produced as a result of radiation can alter or damage the T-cell receptor (TCR) signaling pathway that includes CD3, thus making the cells unresponsive to antigen.

In this study, we are trying to find out whether this damage is at the TCR-CD3 level or at a downstream level. C57BL/6 mice were γ-irradiated (57^Co) to total doses of 0 and 0.049 gray (Gy) over a period of ~8 days (0.0002 Gy/hr) and subsequently exposed to simulated solar flare protons (SF). The protons were delivered over 36h and the dose rate profile mimicked the September 1989 solar flare. Proton energies ranged from 25 to 215 MeV and were delivered in 10 MeV increments; a 2 Gy entrance dose was measured. At the end of irradiation, mice were euthanized in 100% CO_2, and spleens were harvested. T lymphocytes were activated with anti-CD3 by using anti-CD3 monoclonal antibodies coated plates (BD Bioscience). Cytokines/chemokines were quantified by ELISA method using Luminex (Mouse Cytokine/Chemokine premixed Lincoplex kit). Results from the experiment are shown in the table below.

Cytokine/ Chemokine	LDR	SF	LDR + SF
IFN-γ	↑	↑	↑
GM-CSF	↑	↑	↑
MIP-1α	↓	↓	↓
IL-9	↓	↓	↓
IL-7	↓	=	↓
RANTES	=	↑	↑
TNF-α	=	↑	↑
IL-1α	=	↑↑	=

key: ▼ Significantly lower than the non-irradiated control group; P<0.005.
▲▲ Significantly higher than the LDR group; P<0.005
▲ Significantly higher than the non-irradiated control group; P<0.005.
=. No significant difference.
Interleukin (IL), Interferon gamma (IFN-γ), Granulocyte/macrophage colony-stimulating factor (GM-CSF), Murine macrophage inflammatory proein1 alpha (MIP-1α), Regulated on Activation Normal T Expressed and Secreted (RANTES), Tumor necrotic factor alpha (TNF-α), Monocyte chemotactic protein-1 (MCP-1).Interferon gamma inducible protein 10 (IP-10), Keratinocyte-derived chemokine (KC), Granulocyte colony-stimulating factor (G-CSF).

There were no significant differences among groups in MCP-1, IP-10, KC, G-CSF. IL-1β, IL-12, IL-4, IL-5, IL-6, IL-10, IL-12, IL-13, IL-15, and IL-17.

In conclusion, we can say that secretion of IFN-γ and GM-CSF are upregulated, and MIP-1α and IL-9 are downregulated irrespective of the type of radiation used. Simulated solar flare protons upregulated RANTES and TNF-α, and LDR cancelled out the effect of SF on IL-1α. IL-7 was decreased in the LDR and LDR+SF group, possibly reflecting decreased ability to replenish normal functional T and B cells. In the case of T cells, this latter finding suggests altered TCR gene rearrangement.

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